IN THE CLAIMS

In compliance with the practice guidelines for making amendments, Applicants present all pending claims with status indicators.

Claims 1-9, 11-18 are pending. Claims 10 and 19-36 were withdrawn from consideration as being drawn to a non-elected invention and species.

Please amend claims 2-4, 6-7 and 13 and add new claims 37-42.

Claim 1. (Original) A method for regulating a cell-mediated immune response, comprising administering:

a. a first agent which blocks a CD28/CTLA4/B7-mediated signal by binding CD28, CTLA4 or B7;

b. a second agent which blocks a CD40/CD154-mediated signal by binding either CD40 or CD154; and

c. a third agent which blocks an adhesion molecule-mediated interaction by binding to LFA-1, ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesin-1,

whereby blocking by the first, second and third agents regulates a cell-mediated immune response.

Claim 2. (Currently amended) ~~A method for treating an immune system disease by regulating a cell-mediated immune response by the method of claim 1.~~ The method of claim 1, wherein regulating a cell-mediated immune response by blocking said CD28/CTLA4/B7-mediated signal, said CD40/CD154-mediated signal and said adhesion molecule-mediated interaction, treats an immune system disease in a subject.

Claim 3. (Currently Amended) A method for ~~inhibiting~~ treating an immune system disease in a subject comprising administering to a subject:

a. a first agent which blocks a CD28/CTLA4/B7-mediated signal by binding CD28, CTLA4 or B7;

b. a second agent which blocks a CD40/CD154-mediated signal by binding either CD40 or CD154; and

c. a third agent which blocks an adhesion molecule-mediated interaction by binding to LFA-1, ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesin-1,

whereby blocking the first, second and third agents ~~inhibits~~ treats an immune system disease.

Claim 4. (Currently amended) A method for inhibiting transplant rejection in a subject, comprising administering to ~~a~~ the subject having a transplant:

a. a first agent which blocks a CD28/CTLA4/B7-mediated signal by binding CD28, CTLA4 or B7;

b. a second agent which blocks a CD40/CD154-mediated signal by binding either CD40 or CD154; and

c. a third agent which blocks an adhesion molecule-mediated interaction by binding to LFA-1, ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesin-1,

whereby blocking the first, second and third agents inhibits a cell-mediated immune response to the transplant rejection.

Claim 5. (Original) The method of claim 1, 3 or 4, wherein the first agent binds a B7 and is a soluble CTLA4 molecule, a soluble CD28 molecule, or an anti-B7 monoclonal antibody; wherein the first agent binds a CTLA4 and is an anti-CTLA4 monoclonal antibody or a soluble B7 molecule; and/or wherein the first agent binds a

CD28 and is an anti-CD28 monoclonal antibody or a soluble B7 molecule.

Claim 6. (Currently amended) The method of claim 5, wherein the soluble CTLA4 molecule is CTLA4Ig (ATCC 68629) or L104EA29YIg (ATCC PTA-2104); wherein the soluble CD28 molecule is CD28Ig (ATCC 68628); wherein the soluble B7 molecule is B7Ig (ATCC 68627); wherein the anti-B7 monoclonal antibody is ATCC HB-253, ATCC CRL-2223, ATCC CRL-2226, ATCC HB-301 or ATCC HB-11341; wherein the anti-CTLA4 ~~monclonal~~ monoclonal antibody is ATCC HB-304; and wherein the anti-CD28 monoclonal antibody is mAb 9.3.

Claim 7. (Currently amended) The method of claim 1, 3 or 4, wherein the second agent binds a CD154 and is an anti-CD154 monoclonal antibody, and/or wherein the second agent binds CD40 and is an anti-CD40 monoclonal antibody.

Claim 8. (Original) The method of claim 7, wherein the anti-CD154 monoclonal antibody is MR1, ATCC HB-10916, ATCC HB-12055 or ATCC HB-12056 and wherein the anti-CD40 monoclonal antibody is ATCC HB-9110.

Claim 9. (Original) The method of claim 1, 3 or 4, wherein the third agent binds LFA1 and is an anti-LFA-1 monoclonal antibody; wherein the third agent binds ICAM-1 and is an anti-ICAM-1 antibody; wherein the third agent binds ICAM-2 and is an anti-ICAM-2 antibody; wherein the third agent binds ICAM-3 and is an anti-ICAM-3 antibody; wherein the third agent binds α-actinin and is an anti-α-actinin antibody; wherein the third agent binds filamin and is an anti-filamin antibody; wherein the third agent binds cytohesin-1 and is an anti-cytohesin-1 antibody; wherein the third agent binds CD18 and is an anti-CD18 antibody; and/or wherein the third agent binds CD11a and is an anti-CD11a antibody.

Claim 10. (Withdrawn) The method of claim 1, 3 or 4, wherein the third agent binds

any of ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesion-1 and is a soluble LFA-1; and/or wherein the third agent binds to LFA-1 and is soluble ICAM-1, soluble ICAM-2, soluble ICAM-3, soluble α-actinin, soluble filamin or soluble cytohesin-1.

Claim 11. (Previously amended) The method of claim 9, wherein the anti-LFA-1 monoclonal antibody is ATCC HB-9579 or ATCC TIB-213; wherein the anti-ICAM-1 monoclonal antibody is ATCC CRL-1878 or ATCC HB-233; wherein the anti-CD11a monoclonal antibody is M17/5.2 (ATCC TIB-237), ATCC HB-202, ATCC HB-244 or ATCC TIB-217; wherein the anti-CD18 monoclonal antibody is ATCC HB-203, ATCC HB-226 or ATCC TIB-218; and wherein the anti-α-actinin monoclonal antibody is ATCC CRL-2252.

Claim 12. (Original) The method of claim 1, 3 or 4, wherein the third agent which blocks the adhesion molecule-mediated interaction blocks an LFA-1/ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin, cytohesion-1 interaction.

Claim 13. (Currently amended) The method of claim 2 or 3, wherein ~~an~~ the immune system disease is selected from the group consisting of graft versus host disease (GVHD), psoriasis, immune disorders associated with graft transplant rejection, T cell lymphoma, T cell acute lymphoblastic leukemia, testicular angiocentric T cell lymphoma, benign lymphocytic angiitis, lupus (e.g. lupus erythematosus, lupus nephritis), Hashimoto's thyroiditis, primary myxedema, Graves' disease, pernicious anemia, autoimmune atrophic gastritis, Addison's disease, diabetes (e.g. insulin dependent diabetes mellitis, type I diabetes mellitis), good pasture's syndrome, myasthenia gravis, pemphigus, Crohn's disease, sympathetic ophthalmia, autoimmune uveitis, multiple sclerosis, autoimmune hemolytic anemia, idiopathic thrombocytopenia, primary biliary cirrhosis, chronic action hepatitis, ulceratis colitis, Sjogren's syndrome, rheumatic diseases (e.g. rheumatoid arthritis), polymyositis, scleroderma, and mixed connective tissue disease.

Claim 14. (Original) The method of claim 1, 3 or 4, wherein the first, second and third agents are administered locally or systemically.

Claim 15. (Original) The method of claim 1, 3 or 4, wherein the first, second and third agents are administered sequentially or concurrently and in any order.

Claim 16. (Original) The method of claim 3 or 4, wherein the subject is selected from the group consisting of human, monkey, ape, dog, cat, cow, horse, rabbit, mouse and rat.

Claim 17. (Currently Amended) A method for ~~regulating~~ treating an immune system disease by blocking a cell-mediated immune response with:

a. a first agent which is a soluble CTLA4; and
b. a second agent which is an anti-CD154 monoclonal antibody; and
c. a third agent which is an anti-LFA-1 monoclonal antibody,

whereby the first, second and third agents ~~inhibits~~ treats the cell-mediated immune disease.

Claim 18. (Original) A method for inhibiting allograft transplant rejection by blocking a cell-mediated immune response with:

a. a first agent which is a soluble CTLA4; and
b. a second agent which is an anti-CD154 monoclonal antibody; and
c. a third agent which is an anti-LFA-1 monoclonal antibody,

wherein the first, second and third agents inhibits the cell-mediated immune response to the transplant.

Claim 19. (Withdrawn) A pharmaceutical composition comprising a first, second and third agent, and wherein

a. the first agent blocks a CD28/CTLA4/B7-mediated signal by binding CD28, CTLA4 or B7,
b. the second agent blocks a CD40/CD154-mediated signal by binding either CD40 or CD154, and
c. the third agent blocks an LFA-1/ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesin-1 interaction.

Claim 20. (Withdrawn) A kit for treating transplant rejection, said kit comprising an effective amount of a first agent, a second agent and a third agent, and

a. the first agent blocks a CD28/CTLA4/B7-mediated signal by binding CD28, CTLA4 or B7;
b. the second agent blocks a CD40/CD154-mediated signal by binding either CD40 or CD154; and
c. the third agent blocks an LFA-1/ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesin-1 interaction.

Claim 21. (Withdrawn) The pharmaceutical composition of claim 19 further comprising at least one immunosuppressive agent, wherein the immunosuppressive agent is selected from the group consisting of corticosteroids, nonsteroidal antiinflammatory drugs (e.g. Cox-2 inhibitors), cyclosporin prednisone, azathioprine, methotrexate, TNFα blockers or antagonists, infliximab, any biological agent targeting an inflammatory cytokine, hydroxychloroquine, sulphasalazopryine, gold salts, etanercept, and anakinra.

Claim 22. (Withdrawn) The pharmaceutical composition of claim 19, wherein the first agent binds a B7 and is a soluble CTLA4 molecule, a soluble CD28 molecule, or an anti-B7 monoclonal antibody; wherein the first agent binds a CTLA4 and is an anti-CTLA4 monoclonal antibody or a soluble B7 molecule; and/or wherein the first agent binds a CD28 and is an anti-CD28 monoclonal antibody,or a soluble B7 molecule.

Claim 23. (Withdrawn) The pharmaceutical composition of claim 22, wherein the soluble CTLA4 molecule is CTLA4Ig (ATCC 68629) or L104EA29YIg (ATCC PTA-2104); wherein the soluble CD28 molecule is CD28Ig (ATCC 68628); wherein the soluble B7 molecule is B7Ig (ATCC 68627); wherein the anti-B7 monoclonal antibody is ATCC HB-253, ATCC CRL-2223, ATCC CRL-2226, ATCC HB-301 or ATCC HB-11341; wherein the anti-CTLA4 monclonal antibody is ATCC HB-304; and wherein the anti-CD28 monoclonal antibody is ATCC HB 11944 or mAb 9.3.

Claim 24. (Withdrawn) The pharmaceutical composition of claim 19, wherein the second agent binds a CD154 and is an anti-CD154 monoclonal antibody, and/or wherein the second agent binds CD40 and is an anti-CD40 monoclonal antibody.

Claim 25. (Withdrawn) The pharmaceutical composition of claim 24, wherein the anti-CD154 monoclonal antibody is MR1, ATCC HB-10916, ATCC HB-12055 or ATCC HB-12056 and wherein the anti-CD40 monoclonal antibody is ATCC HB-9110.

Claim 26. (Withdrawn) The pharmaceutical composition of claim 19, wherein the third agent binds LFA1 and is an anti-LFA-1 monoclonal antibody; wherein the third agent binds ICAM-1 and is an anti-ICAM-1 antibody; wherein the third agent binds ICAM-2 and is an anti-ICAM-2 antibody; wherein the third agent binds ICAM-3 and is an anti-ICAM-3 antibody; wherein the third agent binds α-actinin and is an anti-α-actinin antibody; wherein the third agent binds filamin and is an anti-filamin antibody; wherein the third agent binds cytohesin-1 and is an anti-cytohesin-1 antibody; wherein the third agent binds CD18 and is an anti-CD18 antibody; and/or wherein the third agent binds CD11a and is an anti-CD11a antibody.

Claim 27. (Withdrawn) The pharmaceutical composition of claim 19, wherein the third agent binds any of ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesion-1 and is a soluble LFA-1; and/or wherein the third agent binds to LFA-1 and is soluble

ICAM-1, soluble ICAM-2, soluble ICAM-3, soluble α-actinin, soluble filamin or soluble cytohesin-1.

Claim 28. (Withdrawn) The pharmaceutical composition of claim 27, wherein the anti-LFA-1 monoclonal antibody is ATCC HB-9579 or ATCC TIB-213; wherein the anti-ICAM-1 monoclonal antibody is ATCC CRL-1878 or ATCC HB-233; wherein the anti-CD11a monoclonal antibody is M17/5.2 (ATCC TIB-237), ATCC HB-202, ATCC HB-244 or ATCC TIB-217; wherein the anti-CD18 monoclonal antibody is ATCC HB-203, ATCC HB-226 or ATCC TIB-218; and wherein the anti-α-actinin monoclonal antibody is ATCC CRL-2252.

Claim 29. (Withdrawn) The kit of claim 20 further comprising at least one immunosuppressive agent, wherein the immunosuppressive agent is selected from the group consisting of corticosteroids, nonsteroidal antiinflammatory drugs (e.g. Cox-2 inhibitors), cyclosporin prednisone, azathioprine, methotrexate, TNFα blockers or antagonists, infliximab, any biological agent targeting an inflammatory cytokine, hydroxychloroquine, sulphasalazopryine, gold salts, etanercept, and anakinra.

Claim 30. (Withdrawn) The kit of claim 20, wherein the first agent binds a B7 and is a soluble CTLA4 molecule, a soluble CD28 molecule, or an anti-B7 monoclonal antibody; wherein the first agent binds a CTLA4 and is an anti-CTLA4 monoclonal antibody or a soluble B7 molecule; and/or wherein the first agent binds a CD28 and is an anti-CD28 monoclonal antibody or a soluble B7 molecule.

Claim 31. (Withdrawn) The kit of claim 30, wherein the soluble CTLA4 molecule is CTLA4Ig (ATCC 68629) or L104EA29YIg (ATCC PTA-2104); wherein the soluble CD28 molecule is CD28Ig (ATCC 68628); wherein the soluble B7 molecule is B7Ig (ATCC 68627); wherein the anti-B7 monoclonal antibody is ATCC HB-253, ATCC CRL-2223, ATCC CRL-2226, ATCC HB-301 or ATCC HB-11341; wherein the anti-

CTLA4 monclonal antibody is ATCC HB-304; and wherein the anti-CD28 monoclonal antibody is ATCC HB 11944 or mAb 9.3.

Claim 32. (Withdrawn) The kit of claim 20, wherein the second agent binds a CD154 and is an anti-CD154 monoclonal antibody, and/or wherein the second agent binds CD40 and is an anti-CD40 monoclonal antibody.

Claim 33. (Withdrawn) The kit of claim 32, wherein the anti-CD154 monoclonal antibody is MR1, ATCC HB-10916, ATCC HB-12055 or ATCC HB-12056 and wherein the anti-CD40 monoclonal antibody is ATCC HB-9110.

Claim 34. (Withdrawn) The kit of claim 20, wherein the third agent binds LFA1 and is an anti-LFA-1 monoclonal antibody; wherein the third agent binds ICAM-1 and is an anti-ICAM-1 antibody; wherein the third agent binds ICAM-2 and is an anti-ICAM-2 antibody; wherein the third agent binds ICAM-3 and is an anti-ICAM-3 antibody; wherein the third agent binds α-actinin and is an anti-α-actinin antibody; wherein the third agent binds filamin and is an anti-filamin antibody; wherein the third agent binds cytohesin-1 and is an anti-cytohesin-1 antibody; wherein the third agent binds CD18 and is an anti-CD18 antibody; and/or wherein the third agent binds CD11a and is an anti-CD11a antibody.

Claim 35. (Withdrawn) The kit of claim 20, wherein the third agent binds any of ICAM-1, ICAM-2, ICAM-3, α-actinin, filamin or cytohesion-1, and is a soluble LFA-1 or wherein the third agent binds to LFA-1 and is soluble ICAM-1, soluble ICAM-2, soluble ICAM-3, soluble α-actinin, soluble filamin or soluble cytohesin-1.

Claim 36. (Withdrawn) The kit of claim 35, wherein the anti-LFA-1 monoclonal antibody is ATCC HB-9579 or ATCC TIB-213; wherein the anti-ICAM-1 monoclonal antibody is ATCC CRL-1878 or ATCC HB-233; wherein the anti-CD11a monoclonal

antibody is M17/5.2 (ATCC TIB-237), ATCC HB-202, ATCC HB-244 or ATCC TIB-217; wherein the anti-CD18 monoclonal antibody is ATCC HB-203, ATCC HB-226 or ATCC TIB-218; and wherein the anti-α-actinin monoclonal antibody is ATCC CRL-2252.

Claim 37. (New) The method of claim 1, wherein blocking by the first, second and third agents inhibits a cell-mediated immune response.

Claim 38. (New) The method of claim 1, 3 or 4, wherein CD28 and/or CTLA4 are on T cells, B7 is on B cells, LFA-1 is on LFA-1 positive cells, ICAM-1 is on ICAM-1 positive cells, ICAM-2 is on ICAM-2 positive cells, ICAM-3 is on ICAM-3 positive cells, α-actinin is on α-actinin positive cells, filamin is on filamin positive cells and cytohesin-1 is on cytohesin-1 positive cells.

Claim 39. (New) The method of claim 1, 3, 4, or 17 further comprising an additional immunosuppressive agent.

Claim 40. (New) The method of claim 38, wherein the immunosuppressive agent is selected from a group consisting of corticosteroids, nonsteroidal antiinflammatory drugs, cyclosporine, prednisone, azathioprine, methotrexate, TNFα blockers or antagonists, infliximab, an agent targeting an inflammatory cytokine, hydroxychloroquine, sulphasalazopryine, gold salts, etanercept, and anakinra.

Claim 41. (New) A method for treating an immune system disease by blocking a cell-mediated immune response with:

a. a first agent which is a soluble CTLA4; and
b. a second agent which is an anti-CD40 monoclonal antibody; and
c. a third agent which is an anti-LFA-1 monoclonal antibody,

whereby the first, second and third agents treats the cell-mediated immune disease.

Claim 42. (New) A method for inhibiting allograft transplant rejection by blocking a cell-mediated immune response with:

a. a first agent which is a soluble CTLA4; and

b. a second agent which is an anti-CD40 monoclonal antibody; and

c. a third agent which is an anti-LFA-1 monoclonal antibody,

wherein the first, second and third agents inhibits the cell-mediated immune response to the transplant.